

A	B	IV	SN
SKD3 EEHPLV-FLFLGSSGIGKTELAKQTAKYMHDAKKGFIRLDMSSEFQERHEYAKF [GSPPGYIGHEEGQQ-LTKKLKGCPNAVVLFDVKAHPDYLITMLQLFDEGR]	HSP-101 PQQPTGSFLFLGPTGVGKTELAKALAEQLF-DNEQLVRDMSEYMEQHSYSRLLGAPPGYVGHHEEGQQ-LTEAVRRPYSWVLFDEVEKAHTSVFNLLQVLDDGRL	TorsinA PKKPLTLSL-HGWTGTGKNFVSKIIAENIYEGLN-----SDYVHLFVATLHFPHASNITLYKDQLQLWIRGNVSACARSIFIDEMDKHAGLI DAIKPFLD-----	TorsinB PKKPLTLSL-HGWTGTGKNFVSKIIAENIYEGLN-----SNFVHLFVSTLHFPHQEOKTIKYDQLQKWI RGNSACANSVFIDEMDKLHPGII DAIKPFLD-----
TorpCel PRKPLVLSF-HGYTGSGKKNVAEIIIAANNTRFLGLR-----STFVQHIVATNDFPDKNKLEEEYQVELRNRIITTVQKCQRSTIFIDEADKLPEQQLGAIAKPFLD-----	Torpi PSKPLVLSL-HGWTGTGKSYSSLLAQHFLFRGLR-----SPHVHFSPIIHFPHSRTEQYKRELKSSWQGNLTACERSLSSLFDEMDKLPPGLEMVLPQFLG-----	Torp2 SKD3 TDGKCKTIDICKDAIFIMTSNVAASDEIAQHALQLRQEALEMSRNRIAENLGDVQMSDKITISKNFKENVIRPILKAHFRRDEFGLRINEIVYFLPFCHSELIGQLVNLKEL	HSP-101 TDGQGRTVDFRNTVIMTSNLGAELLS-GLSGKC-TMQWARDR-----VMQEVRQQ-FRPPELLNRLEDIVWFDPLSHDLQRVARLQM
TorsinA YDLYDGVSYQKAMIFILSNAGAERITDVALDFW-----RSGKREDIKLKDIEHALSVSFNNK--NSGFWHSSLIDRNLIDYFVPELPLEYKHLKMCIRVEM	TorsinB YYEQDVGSYXKAIFIFLSNAGGDILITKTAIDFW-----RAGRREDIQLKDIEPVLSVGFGNNK--HSGLWHSGLIDKNLIDYFIPFLPLEYRHVKMCVRAEM	TorpCel YYSTISGVDFRRSIFILSNKGGEFARIITKEQY-----ESGYPREQRLAFTERELMNFSYNEK---GGLQMSSELISNHLIDHFPFLPLQREHVRSVGAYL	Torpi PSWVYGTNYRKAIIFISNAGGEQINQVALEAW-----RTNRDREISLQVEPVISRAYMDNP--QHGFWRSGIMEEHLDAVVPFLPLQRLHHVRHCVLNEL
Torp2 RAPEXXGLSLXWTIFLFSNLRGDIINEVVLKLL-----KAGWSREEITMELHEPHLQAEIVDDH--RQWLWHSRLVKENLIDYFIPFLPLEYRHVRLCARDAF			

FIG. 4C

FIG. 5B

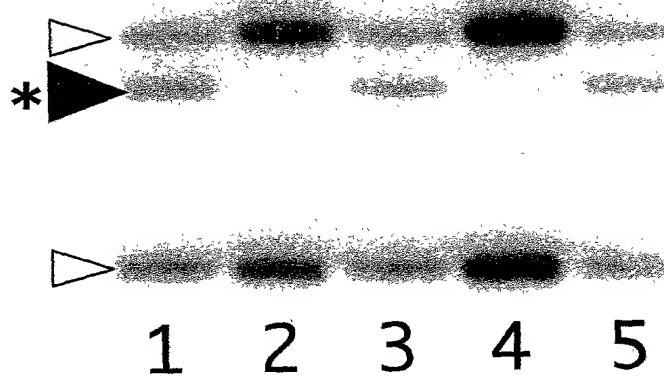


FIG. 5C

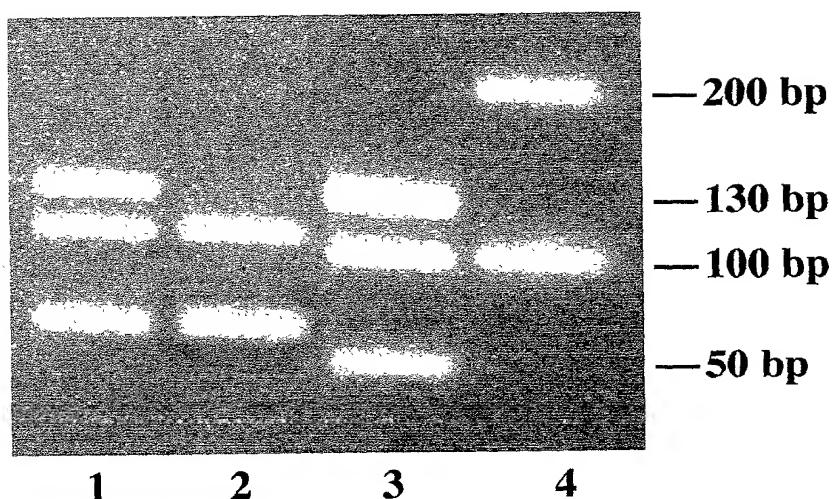
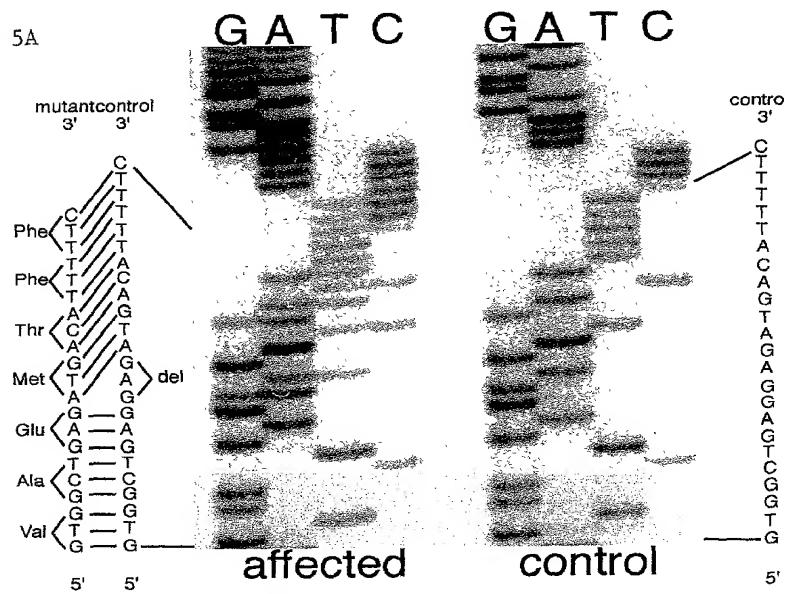


FIG. 5A



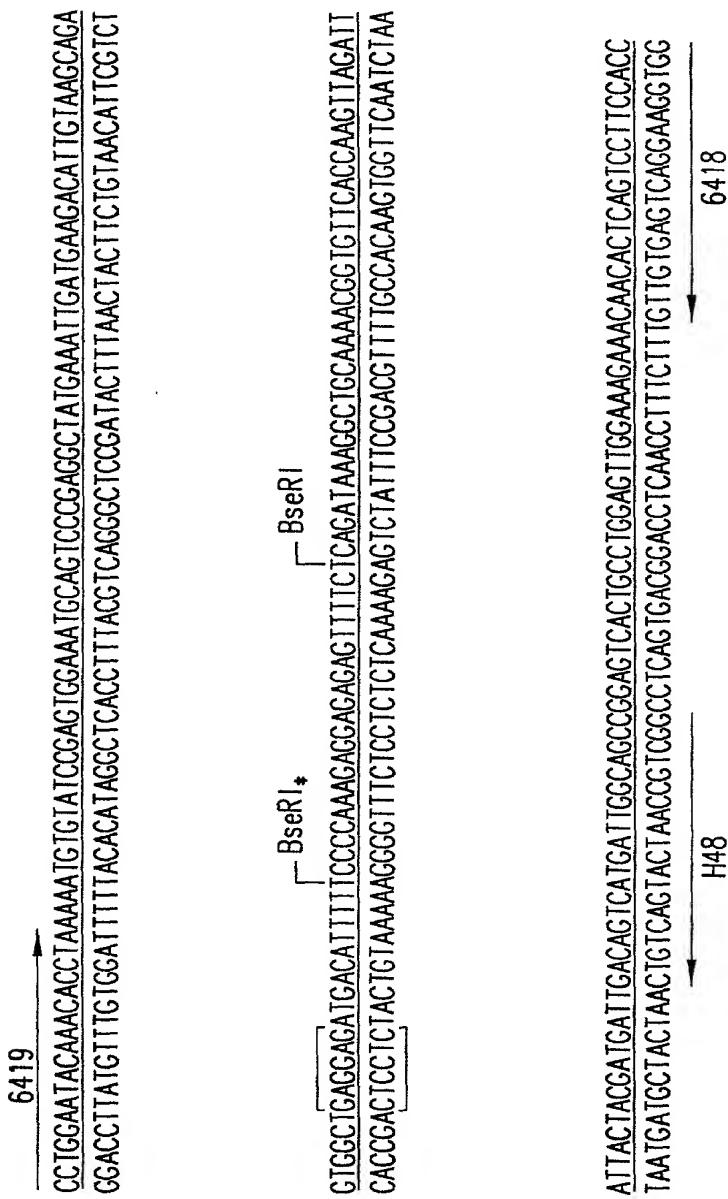


FIG. 5D

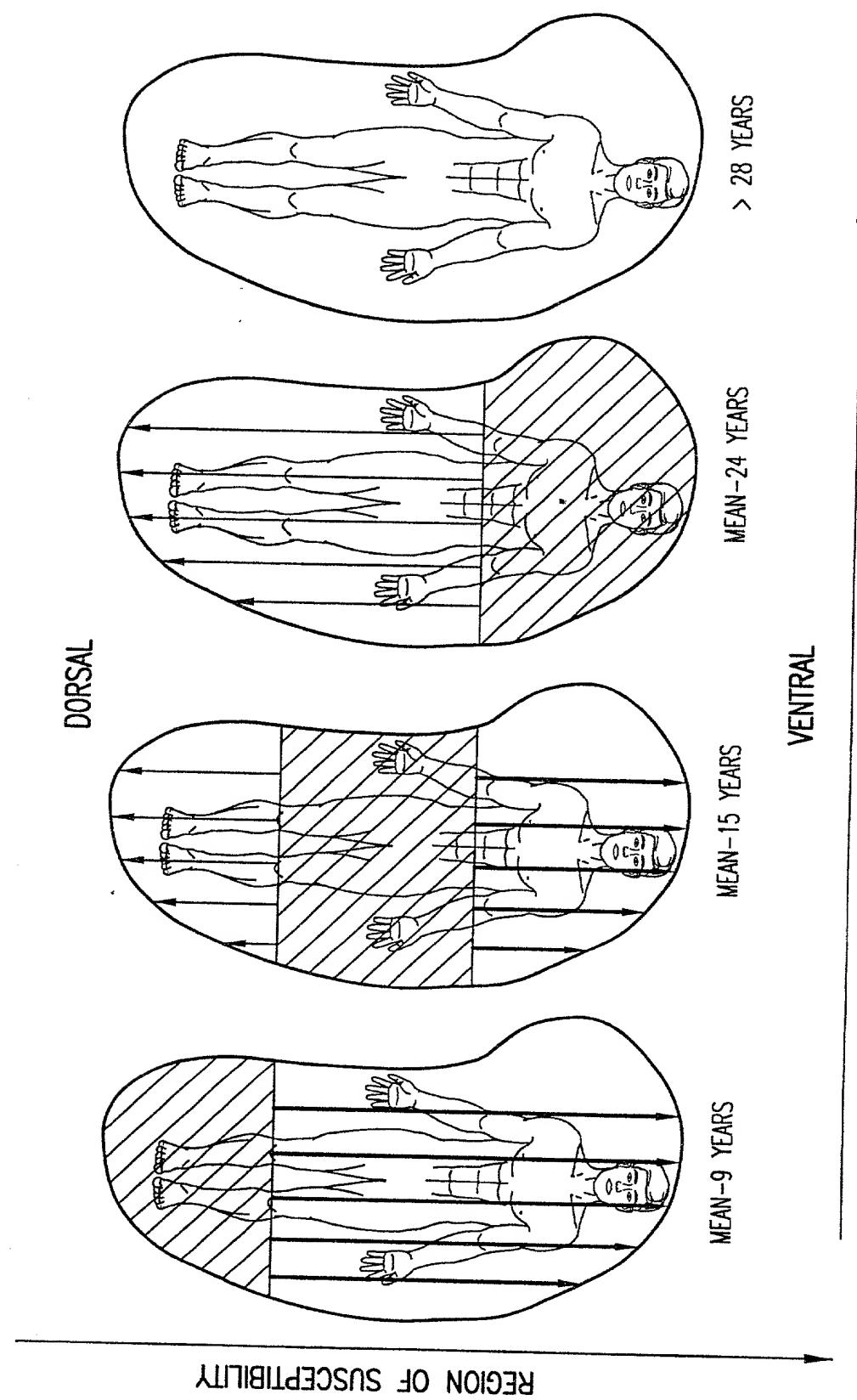


FIG. 6

Docket No.: 0838.1001-009
"Torsin, Torsin-Related Genes and Methods..."
Inventors: Laurie J. Ozelius *et al.*

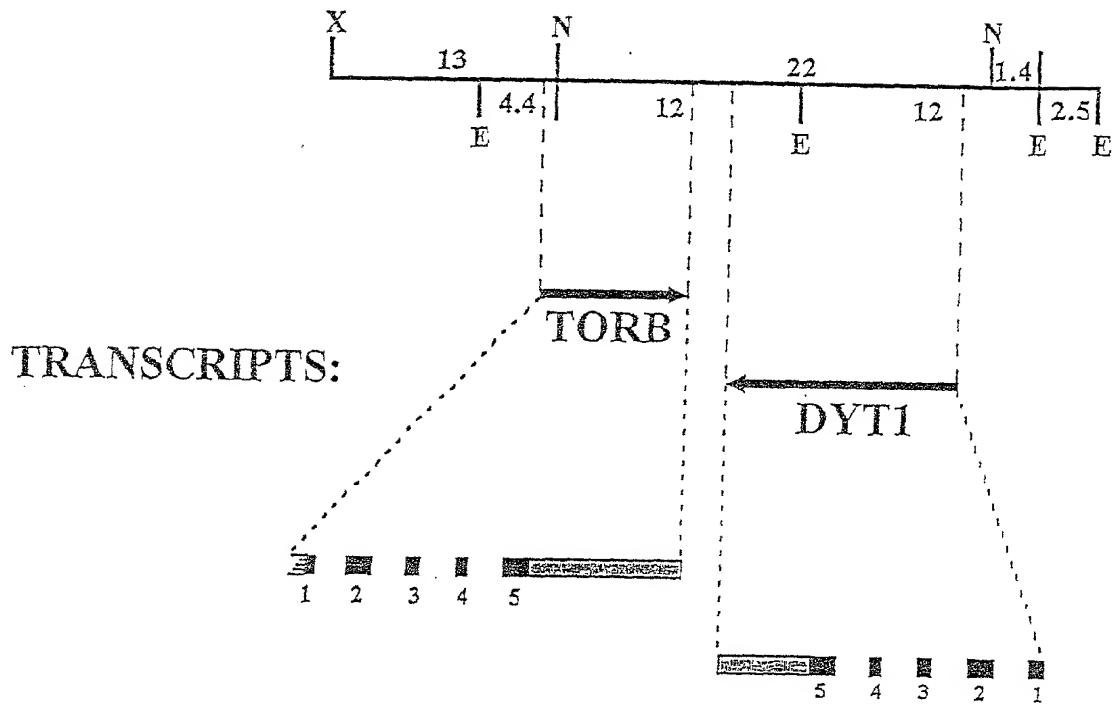


FIG. 7

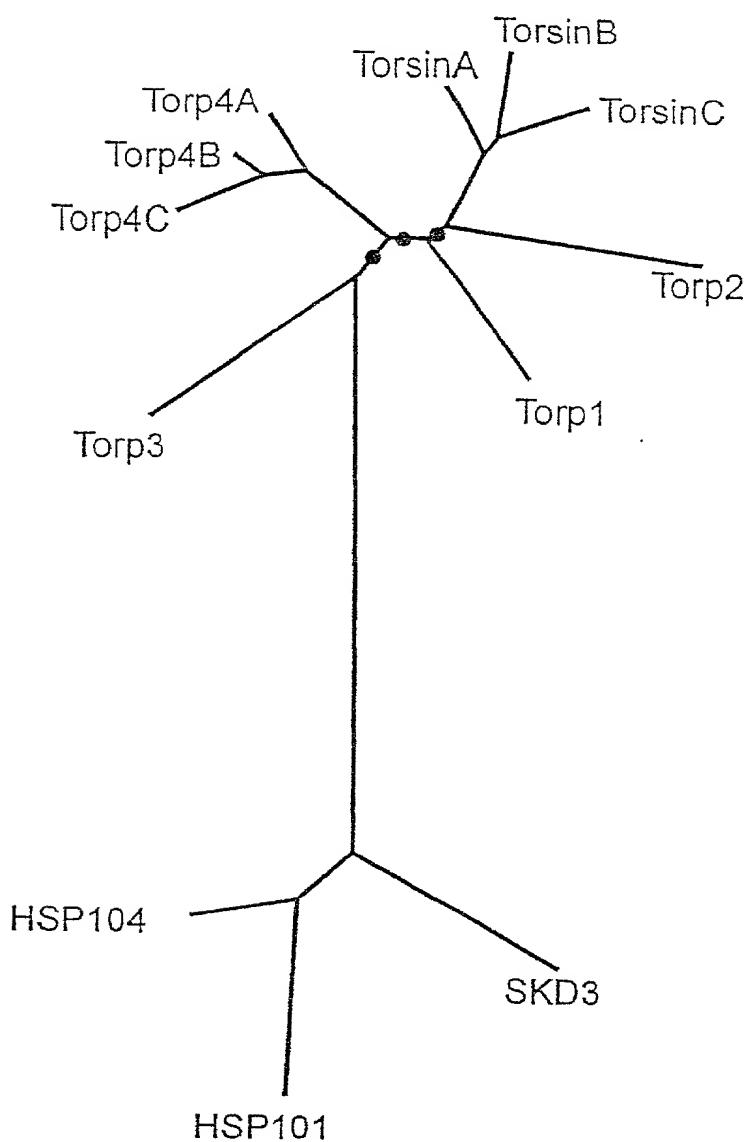


FIG. 8

FIG. 9A

DYT1						
Exon	Size (bp)	3'end of exon	5' splice site (SEQ ID NO)	Intron (kb) ^a	3' splice site (SEQ ID NO)	5' end of exon (SEQ ID NO)
1	178	...CGG GAG G R E A	GTAAGGCTGGG... (67)	1.2	...TCCTTCCCAG (71)	CA CTG CAG AAG... (75)
2	266	...TTG TAC AAG L Y K	GCAAGGGATGG... (68)	1.5	...TTAAATTCAAG (72)	L G K
3	176	...TTCTCTCAG F L S	GTAAGGGTCAG... (69)	0.097	...TGTTTTCAG (73)	D Q L
4	128	...AAG AAC AG K N S	GTGAGTAGGG... (70)	4	...TTCTTCCCAG (74)	CAAT GCT GGA... (76)
5	251	...GAT GAT TGA D D *			T GGCTTC TGG... (77)	N A G

FIG. 9B

TORB						
Exon	Size (bp)	3'end of exon	5' splice site (SEQ ID NO)	Intron (kb) ^a	3' splice site (SEQ ID NO)	5' end of exon (SEQ ID NO)
1	n.d.	...GCT TCG G A S A		n.d.	...GTTCTTGCAG (81)	CT CTC AAG CTG... (85)
2	266	...CTG TAC CAG L Y Q	GCAAGAGAAC... (78)	3	...GTTGGTCCAG (82)	L K L
3	176	...TTCTCTCAG F L S	GTCAAGGGAA... (79)	1.8	...GCAAACCTCAAG (83)	D Q L
4	128	...AAA CAC AG K H S	GTGAGTCCAC... (80)	.31	...TGTTCTGCAG (84)	CAAT GCA GGC... (86)
5	242	...TTC CAC TGA F H *			T GGC CTG TGG... (87)	N A G

*Sizes of introns were approximated by gel resolution of PCR products

Docket No.: 0838.1001-009
 "Torsin, Torsin-Related Genes and Methods..."
 Inventors: Laurie J. Ozelius *et al.*

Type	Number of Individuals	Age of onset yrs	Site of onset ^a (no.)	Sites involved (no.)
Early onset:				
AJ	5	6, 8, 10, 19	A(4), ANL(1)	A(7), N(3), T(1), L(2)
NJ	12	3, 6(2), 8, 9, 10, 11, 13, 14(2), 16, 18	A(9), AU(1)	A(20), G(9),
Potential homozygosity:				
AJ ^b	5	4, 6, 7, 26, 35	L(4), M(1)	L(4), M(1), N(2), P(1),
Late onset:				
AJ	1	66	U	T(1), U(1), H(2)
			U	

* Body sites: U=upper face, F=lower face, J=jaw, T=tongue, P=pharynx, L=larynx, S=speech, swallowing, A=arm, K=trunk, G=leg, N=neck, H=hearing loss.
 (no.=Number of individuals in group with that site affected.)

^b Three of these individuals had all known AJ ancestors, one was 7/8 AJ, and one was 1/2 AJ.

<u>Sample number</u>	Genotype			
	D9S2160 ^a	D9S2161	D9S63	D9S2162
18843	3,4	2,2	8,8	4,4
13709	4,4	2,6	14,14	NT ^b
14122 ^c	3,3	4,4	0,0	5,5
13945	4,4	1,5	18,18	NT ^b
14040	2,5	1,2	16,16	2,4

^a Markers listed from centromere to telomere: D9S2160 - <40 kb - D9S2161 - 150 kb - D9S63 - 130 kb - D9S2162 (Ozelius et al., 1997a).

^b Position of DYT1 gene

^c Not tested.

This individual had onset at 7 years in the arm with eventual involvement of the arm and neck and a positive family history of movement disorder (father with tremor). He was also apparently homozygous for markers D9S159-D9S2158-D9S2159, which are proximal to DS2160 (total region of 100 kb).

FIG. 11

FIG. 12A

Intron Primers Used to Amplify DYT1 Exons			
Exon	Primer Sequence (5' → 3')	SEQ. ID NO.:	Product Size (bp)*
1	GCAAAACAGGGCTTGTACCG	(SEQ. ID NO.: 30)	
	AGTAGAGACGCCGGTAGATG	(SEQ. ID NO.: 31)	
	GCGTCTCTACTGCCTCTTCG	(SEQ. ID NO.: 32)	
	ATGCCCTGGCCTAGTTTAG	(SEQ. ID NO.: 33)	
2	GGTTTCGCAAGGTGCTTGGGA	(SEQ. ID NO.: 34)	408
	GGGATTCCAAACTTCCATCC	(SEQ. ID NO.: 35)	
3 and 4	TCCATGGGGTTGGTAGGAAC	(SEQ. ID NO.: 36)	804
	GGTGACAGAGTAAAACATCTG	(SEQ. ID NO.: 37)	
5	GACCCCCAGTAGACGTTGT	(SEQ. ID NO.: 38)	640
	GTAAAAAAATCATGAGCCCTGC	(SEQ. ID NO.: 39)	

FIG. 12B

Intron Primers Used to Amplify TORB Exons			
Exon	Primer Sequence (5' → 3')	SEQ. ID NO.:	Product Size (bp)*
1	n.d. [#]		-
2	CCAGAGTTAGTGAGCAGGTC	(SEQ. ID NO.: 40)	526
	GAAGCGTTAAGGACCTCCAC	(SEQ. ID NO.: 41)	
3	ATCTATCTGCCAATTCCAC	(SEQ. ID NO.: 42)	466
	GTCCTGGTAAACAAAGTGCTG	(SEQ. ID NO.: 43)	
4	TGGGGTTACTCTATGTTGGTC	(SEQ. ID NO.: 44)	440
	CTAGCACAGTATGCCCTAAG	(SEQ. ID NO.: 45)	
5	TGAGGAATGTGCTGAGGGTC	(SEQ. ID NO.: 46)	333
	GCTGTCTCCTACCCATCTG	(SEQ. ID NO.: 47)	

*PCR products were generated using oligonucleotides synthesized from intronic sequences, and accordingly the size of each product includes both intron and exon sequence.

#Not done. It was not possible to identify primers which could consistently PCR this exon.

<i>Protein</i>	<i>Organism</i>	<i>Gene</i>	<i>Locus</i>	<i>Accession</i>	<i>UniGene</i>
hTorsinA	human	DYT1	Chr.9, D9S159-D9S164	AF007871	Hs.19261
mTorsinA	mouse			AA230756	Mm.40438
rTorsinA	rat			AA850233	Rn.20041
sTorsinA	pig			AU058534	
hTorsinB	human	TORB	Chr.9, D9S159-D9S164	AF007872	Hs.5091
mTorsinB	mouse			AA596988	
drTorsinC	zebrafish			AA542632	
hTorp1	human	TORP1		AA873275	Hs.59038
mTorp1	mouse			AA981789	Mm.33875
rTorp1	rat			H31561	
hTorp2	human	TORP2		AA150869	Hs.26267
mTorp2	mouse			AA791729	
dmTorp3	fruitfly	EG:84H4.1	DMC84H4	AL031766	
ceTorp4A	nematode	F44G4.1	CEC18E9	P54073	
ceTorp4B	nematode	Y37A1B.12	CEY37A1B	AL023835	
ceTorp4C	nematode	Y37A1B.13	CEY37A1B	AL023835	

FIG. 13

INTRON 1 OF DYT1 GENE

FIG. 14A: Clone 1:
23g14-2-7050.cDNA (Length: 283) SEQ ID NO.: 48

1 gttaggctggg gcgggggctg gaggctgggg ctggggctgg ggctgggcga
51 tggcactagg **gctgaactag** **gaccaggcg**a tggagaatgg aggatggagg
101 ccgggggatg gcaccagggc cgggctagga ctagggctgg agcggggcct
151 gggggctggg gctgggcgt ggcactaggg cgggttgggg ctggggctgg
201 ggctggggga tggagcgggg cccggggctg ggggtggggc tgggggatcg
251 actagggctg gnttaggacc aggccggttgg cat

Bold = primer 4 (reverse sequence) from FIG. 12A
Underline = 5' splice sequence from Intron 1 FIG. 9A

FIG. 14B: Clone 2:
Harvey7-23g14-2.cDNA (Length: 375) SEQ ID NO.: 49

1 ggatggtgga tggaggctgg gggatggcag tagggccggg ctaggactgg
51 ggctggagcg gagttttgggg ctggggctca ggagcggggg ctggggctgg
101 ggctggggct gggggatggc actaggcgag gccggggtag gggtcacatc
151 ccaggaggcg cgggctggc agagctgagt ccgcgggggc cggacccccgg
201 aaggccaagcn gccggcctgc aggatgagggc ctggctccctc ggccatgacc
251 acagacgtgc cagacttaag tacggagacc tgaggagcca ggctgcagtt
301 ggcctacttt ncncctaagct gggggtgtggac cagtggtaac ctccctccgaa
351 gtgggttctg ctctttctag cctag

FIG. 14C: Clone 3:
23g1-Harvey11.cDNA (Length: 439) SEQ ID NO.: 50

1 ccactgcccac tgccaccagt ttgcaccctt aaccctgtt ctgctccatcc
51 caccckaagg cagagccggn gaaaggaaac agtttggtcc ctcctggtcc
101 gctgcggaaag agtctcacca tccttctgtc tcccttagcta gaaaggaggc
151 agaaccaca ttccggaggga ggttaccact ggccacccccc cagcttagcg
201 caaagtaggc caacctgcac gcctggnnct cctcaggntc tgcctactta
251 agtctggcag ctctnnntca tggccgaggt agccaggctc atccctgcagg
301 nnccngccnn ttgnctncc ggggtntcgn nncccccgtac tcagctcgtc
351 cagccggcct ctggatgtga cctaccgctg ctagtgcac ccagccagcc
401 agccagccgt ctagccagcc aactgtctag ccagtctag

FIG. 14D: Clone 4:
23g1-Harvey6.cDNA (Length: 378) SEQ ID NO.: 51

1 ctggaaaaga caaagccaat caggagtggg gaagaaaacac ggcaaaatgt
51 agccacattt acagccata aganagccag caaagccgtc tagcctccaa
101 gcaccttgcg *aaacacctaa* tactgcggc tggtaagctc ctggcccaga
151 ggggacggcg gtccaggng ccctccctt gctggctctg cctattctaa
201 agccctggcc cgnctcccttc cccaaaaagcc ccttgggtgcc actgccactg
251 ccaccanttt gncccccata ccctgtncgt ctccctccac cccaaaggcag
301 atgcggnnngg ngaaaaggaaa canntttggtc cctccctggc ggctcgngga
351 agactcctca ccatccttcc tgtcttcc

Bold = primer 5 from FIG. 12A
Italics = sequence overlap between Clone 4 and Clone 3
Underline = 3' splice site from FIG. 9A

FIG. 14E: Clone 4:
23g1-Harvey6.cDNA (Length: 388) SEQ ID NO.: 88

1 ctqqqaaaqa ctgggaaaaga caaagccaat caggagtggg gaagaaaacac
51 ggcaaaatgt agccacattt acagccata aganagccag caaagccgtc
101 tagcctccaa **gcacaccttgcg** aaacctcaag tactgcggtc tggtaagctc
151 ctggcccaga ggggacggcg gtccagggng ccctccctt gctggtcctg
201 cctattctaa agccctggcc cgnctccctc ccgaaaagcc cttgggtgcc
251 actgcccactg ccaccanttt gcnccccata ccctgtnctg ctccctccac
301 cccaaggcag atgcggnnngg ngaaaaggaaa cantttggtc cttccctggtc
351 ggctcgngga agactcctca ccatccttcc tgtcttcc

Bold = primer 5 from FIG. 12A

Italics = sequence overlap between Clone 4 and Clone 3

Underline = 3' splice site from FIG. 9A

INTRON 2 DYT1 GENE

FIG. 15A: Clone 1:
29a5-6343.cDNA (Length: 400) SEQ ID NO.: 52

```
1      gaatatttac gagggtggtc tgaacagtga ctatgtccac ctgtttgtgg
51     ccacattgct ctttccacat gcttcaaaca tcaccttgc caaggcaagg
101    atggaagttt ggaatccctt cctggatgtc atcggtttt gggctctttt
151    gttgtggat gagatttggg agttctatgt tgaaatgagt gagcccccggaa
201    aacggttcat gtctcagttc cccttggaaa ggtgtagaag ttaagagttt
251    gagatgcgtg gagcagttaa taccatcaa gctttgtgg gggttctgaa
301    aatcgtcca gtgagttatgt agggtcatgg gatttttagag gtggacatga
351    tcaaattccat ctttagagatc aacacatctc actcattttt attttcttat
```

Bold = primer 6 from FIG. 12A

Underline = 5' splice site sequence for intron 2 from FIG. 9A

FIG. 15B: Clone 1:
29a5-6343.cDNA (Length: 402) SEQ ID NO.: 89

```
1      gaatatttac gagggtggtc tgaacagtga ctatgtccac ctgtttgtgg
51     ccacattgct ctttccacat gcttcaaaca tcaccttgc caaggcaagg
101    atggaagttt ggaatccctt cctggatgtc atcggtttt gggctctttt
151    gttgtggat gagatttggg agttctatgt tgaaatgagt gagcccccggaa
201    aacggttcat gtctcagttc cccttggaaa ggtgtagaag ttaagagttt
251    gagatgcgtg gagcagttaa taccatcaa gctttgtgg gggttctgaa
301    aatcgtcca gtgagttatgt agggtcatgg gatttttagag gtggacatga
351    tcaaattccat ctttagagatc aacacatctc actcattttt attttcttat
401    tt
```

Bold = primer 6 from FIG. 12A

Underline = 5' splice site sequence for intron 2 from FIG. 9A

FIG. 15C: Clone 2:
6550-54a5s.cDNA (Length: 418) SEQ ID NO.: 53

```
1      tttggagtga gacaggactg ggttcagggtc ccagctctgc cacatatagt
51     cttgggcaag tggagtaagc gctctctgtc cctcagttcc ctcattctgt
101    aaatgagaac gatagtgccc actccatggg gttggtagga acaaagaaga
151    ttttgggcat gtaaagttct tagtgcgcag tgcacagtgg tctgttaagt
201    aagctgcgtt tcttagtggt agaaggagct gattgatggc cctggctgag
251    aactttgtgt tcgccttttc ccttttaat tcaggatcag ttacagttgt
301    ggattcgagg caacgtgagt gcctgtgcga ggtccatctt catatttgat
351    gaaatggata agatgcgtgc aggcctcata gatgccntca anccttcct
401    cgactattat gacctgg
```

Bold = primer 7 from FIG. 12a

Underline = 3' splice sequence for intron 2 from FIG. 9A

Italics = EXON 3 sequence

INTRON 3 DYT1

FIG. 16A: Clone 1:
6202-54a5.cDNA (Length: 198) SEQ ID NO.: 54

```
1   ctcgactatt atgaccctggc ggatggggtc tcctaccaga aagccatgtt
51  catatttctc aggtaaggtc agggcttagga catgatggat gggccccgag
101 cccaaggctc tgagctccag gaaaaaccc tgtccttacc cactgggatttttgcagc
151 gtttgcagc aatgctggag cagaaaggat cacagatgtg tttggatt
```

FIG. 16B: Clone 1:
6202-54a5.cDNA (Length: 200) SEQ ID NO.: 90

```
1   ctcgactatt atgaccctggc ggatggggtc tcctaccaga aagccatgtt
51  catatttctc aggtaaggtc agggcttagga catgatggat gggccccgag
101 cccaaggctc tgagctccag gaaaaaccc tgtccttacc cactgggatttttgcagc
151 gtttgcagc aatgctggag cagaaaggat cacagatgtg gctttggatt
```

Bold = EXON

Underline = sequence from for 5' splice site sequence and 3' splice site sequence, respectively from FIG. 9A

INTRON 4 DYT1

FIG. 17A: Clone 1:
Intron 4-5 prime.cDNA (Length: 535) SEQ ID NO.: 55

1 *GTCTGTGTCG GTTTCAATA ACAAGAACAG* gTGAGTAGGG CCATCCACCG
51 CCAGTCCCCT ATGGTTCTTA ATCCTGCACC CTAAGTGTAA AAAGCATCAG
101 GGTCACTGTC AGCATCACCT GGGAGCTGGG TAGAAAGAAA TGgAGATTCT
151 CAGTCCCCCTT CCGAGTCATG AGGGGAATCT TTGCTGATGA ACTCCAGGTA
201 ACTTTTATGA ACACATAATGT TTGACAAGTG CTGTTTATT TTTATTTTC
251 **AGATAGTTTT** **ACTCTGTCAC** CTAGGCTGGA GTGCAGTGGC GTAACCTTGC
301 CTCACTGCAA CCTCTGCCTC CCGGGCTCAA GCGATTCTTG TGCCTCAGCC
351 TCCTGAGTAG CTGGGATTAC AGGTGCACAC CATGCCAAG CNAATATTT
401 GTATTTTAG TAGAGANGGG GCCCCGTNCA TGTTAACAG GCTGGTCTTG
451 AACTNTTACC TCAGGTGAGT CCNCCACCTC GGCCCTCCAA AGTGCTGGGA
501 TTACAGGCCT GAGCCACTGT GTCTCAGCTT ATTTTT

Italics = EXON sequence

Underline = 5' splice sequence from FIG. 9A

Bold = primer 8 from FIG. 12A

FIG. 17B: Clone 2:
Intron 4-3 prime.cDNA (Length: 1302) SEQ ID NO.: 56

1 *GCCACTCCAA GCTACCATCT GAGATTGTT CCTGCCCTAG AGTGGTAAAG*
51 GCAGTGGTC CGTCTGCCCT CAGCTGTGTC CCCAGGCCA GGGCGTGCCT
101 GGCAACANNA GCAGGCCTCT GAGAACACAGC CTCCCACGTG AGTTCATGAT
151 AGNAAGACAG CCCCTCGTTC CCATTCAAGTG GTTGGTTCTG TTCTTYCCT
201 GGCMATAAGC TCCACTCTGY MRTCAGCCAM ACATTTATTG AGTACCAAGTT
251 GTTGCCAAAG CACTGTTGGG CATGAAAAGC ATTAACCCAG TGAATGAGGA
301 GGAGCTTGGG TTGGGACGGA GCCMCARAAC TACATGGCAG ACCAGAAGGA
351 AATCAGCTCA AGTAGAAARA CACGCATGGG CTCGTGGCG ACGCAGTGTG
401 TGCTGTGTC TCTGGGCTG GGAGGAAGTG TCCTGGATCA GGAGTTCCAG
451 GAGGCCAGGA GGAGTGGACG GGTCACTGCA GAGCCAGCCC GCAATCAGGG
501 GAAGAAAACA CGGCCAAGGC CAGGCCTTCA CGGGGAGCCC AGCGTGGCT
551 GCACATCTGC ACTCTCCAGG CTAGTTTGG TGCCCACATG CTCTGCAGGG
601 TCTGGCACT GTGGCAGCGG CAGCAGGCCT CCCTGTTGCT AGTCCAGCTG
651 CTGAAACTCC AGGGAGAGTC AAAAGTTCC CAAATACAGA GGCGTGGCTG
701 GTAGTCCTTC CGGGGAATTC TTCTTGCTTC CCGCTTCTG TGGAACTCTG
751 CCTTCCCCAC TCTGCCTCTC TGCTTGTTC TGGGCCAG GACCTCTTC
801 CCATCTTCGA TCTCTTAAGT CATACTTGG GAGGCCTCCC CCAGCCGCC
851 GTGTAAAGAG GGCTGTACAC GCTTCTGCTG TCACAGAAGC ATTACAATGT
901 GCAGGTGCCT GTTAACATCT GCCTTCCCCA CTGATCTGGA GCTCCACAAAG
951 GGAGAGGGCA CACCCAGTAG GTATGTGTGG GATGGATAGG AGGGTGGATG
1001 ACACCCAGTA GATGTGTATG GGATGGATAG GAGGGTGGAT GACACCCAGT
1051 AGGTGTGTAT GGGATGGATG GGAGGGTGGG TGACCCCTAG TAGATGTGGG
1101 GGGGTGGGT GGGTGACCCC CAGTAGGGTGT GTGTGGCATG GATAGGTGAC
1151 CCCCAGTACA CGTTTGTGGG ACGGATGGGA GGGTAGGTAA GTGACCCCCA
1201 GGAGGCGTCT ATAGGGCAGG TGGGTGGATG TGGATGAACA GCACCTTGTT
1251 TCTTCTTCCC AGGTGGCTTC TGGCACACCA GCTTAATTGA CCGGAACCTC
1301 AT

Bold = primer 9 in FIG. 12A

Underline is 3' splice site sequence from FIG. 9A

Italics is EXON 5 sequence

INTRON 1 5' from TORB

FIG 18A: Clone 1:
h59-29a5.se (Length: 240) SEQ ID NO.: 57

1 ggagcggccg ctcacgcgtt cgggtacggc gcgcgcgcga gctgtgggtc
51 ggcgcgtcgcc gggggcgccgg ggccgcggggg cgccggaggga cggcctcgta
101 ggcgcctggc acggacccggg cccgtggcat cttagacggcg gtggtcccag
151 ctgggggtggg cggggagcgg atggggcggc cccggaaccg ttcgcnggaa
201 cgcagaagcn gtgcacttgaa acactctcag atcgtgnngc

INTRON 1 3' from TORB

FIG. 18B: Clone 2:
5667s-29a5.Se (Length: 310) SEQ ID NO.: 58

1 gggaccaaag gacgtccgtc gttcccaccc accctaatcg ttgcgcngtc
51 ngttcgtcac ccagttagaga gacttactta cnngtnnacg gaaggaatag
101 tctggggctt **cgcaattact** ggagggttat tagaactttc accgttagcaa
151 actgacggag ccgggatccc acaccgcctg tgggnncgac acgggaccta
201 ttgacacgaa gaacgaaacn gtcgatttt tcacgacgca acgactacgt
251 aaaaattcca gacaaagaga gaaacaagac cccgacaaga acgtcGAGAG
301 TTCGACCTAA

Upper Case Letters = EXON (bottom strand)

Underline = sequence from Table 1

Bold = 2nd primer from FIG. 12B

INTRON 2 5' from TORB

FIG. 19A: Clone 1:
6101-29a5.Se (Length: 401) SEQ ID NO.: 59

1 CAGGAACAAAC AAAATCCCA AGAAACCCT GACCCTTTCC TTACACGGCT
51 GGGCTGGCAC AGGCAAGAAT TTTGTCAGTN AAATTGTGGC TGAAAATCTT
101 CACCCAAAAG GTCTGAAGAG TAACTTTGTC CACCTGTTTG TATCGACTCT
151 GCACTTCCT CATGAGCAGA AGATAAAAAGT ACCAGGgca agagaacccg
201 ctattatctc gtctgcaggc cagtcggact ggtccgggtg **acctgctcac**
251 **taactctggc** ctctgcttct ctttcctttg tggtgctgta gccccccggct
301 ccactgagtt aaggcacact tagtccaggt agttacaaaag ctctcctaca
351 acatttctta cttgggttcca aaacagtcca gtggggtagg ggatgttatt
401 t

Upper Case Letters = EXON
Underline = 5' splice site sequence from FIG. 9B
Bold = 1st primer from FIG. 12B

INTRON 2 3' TORB

FIG. 19B: Clone 2:
29A5-39-11.se (Length: 238) SEQ ID NO.: 60

1 ttctgttaact ggtcCTGGAC CAACCCATGAA AGAAGAAACA GGATGCGAAG
51 CTCAAAGGGC TGCAACCAAGA GGCAGCGCAGG CTCCATCTGC TCCTCATGCA
101 CTGAAGGACG AGGTCAAGAGC TCTTAGAATG GCACCCCTCAC CCCCACTCGC
151 TAGGTAGCAG CTTTTCTAAA ACCTTATCTC TAAAAAGTGG **AAATTGGCAG**
201 **AGATAGATGC** TAAAATGCAG AGAAGTTTT CCTAACTC

Lower Case Letters = EXON
Underline = sequence from Table 1
Bold = primer 3 from FIG. 12B

INTRON 3 5' TORB

FIG. 20A: Clone 1:
39-14-29a5.Se (Length: 391) SEQ ID NO.: 61

1 GGGATCATTG ACGCAATCAA GCCGTTCTA GACTACTACG AGCAGGTTGA
51 CGGAGTGTCT TACCGCAAAG CCATCTTCAT CTTTCTCAGg tcagcggag
101 gcggttttt gggcacaca agcccttcat tctctcaatg ataaaatgag
151 gtcctgagga ccat**cagcac** **tttggttacc** aggacgaaag tgccctgcttg
201 gcacaaggca cttacctact gctttacttt tcctttgccca gtcatcagca
251 tggcacacag tgtgggttgt ggaaatgaac taaagaaata atcactggga
301 caggcgcggt ggctcacacc tgtcaatccn agcactttgg gnaggcatgg
351 cgggcggatc acaggagatc gagacatctg ctaacatgnt g

Upper Case Letters = EXON
Underline = 5' splice site sequence from FIG. 9B
Bold = primer 4 from FIG. 12B

INTRON 3 3' TORB

FIG. 20B: Clone 2:
5665s-54a5.Se (Length: 373) SEQ ID NO.: 62

1 gtaagacaca gagtctttt tnttttttag accgagtntc attnttgttg
51 ccnangctgg agtgcaatgg catgatctcg gctcgctgca acctccacct
101 cccggrrtca aacgattctc ccacctcagc ctccccatgta gctgggattta
151 cagnatgca ccaccattag cctggctaatttttggttttt tttagtagaga
201 **tggggttact** **ctatgttgtt** caggctggcc ttgaactccc gacctcaggt
251 gatctacctg cctcggcctc ccaaagtgtt gggattacag ccatgagcna
301 ccacnsnan cagacncaga agtcttaata tgtgattttt atcttttattt
351 ctctgcaaaa ctcagCAATG CAG

Upper Case Letters = EXON
Underline = 3' splice site sequence from FIG. 9B
Bold = primer 5 from FIG. 12B

INTRON 4 TORB

FIG. 21: Clone 1:
intron4torb.se (Length: 310) SEQ ID NO.: 63

1 gtgagtccac cagggtaaaag gagcccccta actgtccagc agtgagccgt
51 ctgctctttc attgaggttt tgcacaaagc cacaggatcc cactggattt
101 cctcactttg ctaaagtcaag gaatttt**ctt** **agggcatact** **gtgctagaaa**
151 ccagttagtg agtgtccagc tgagtccctcg atgggcttgc tgcacactga
201 caagagacnc tctcaagggg tacggacat**g** **aggaatgtgc** **tgagggtcgg**
251 gactggagct tggccaggtg gcggtggtgg cagggaaaccc agctgtgtct
301 tgttctgcag

Underline = 5' splice site sequence from FIG. 9B

Bold = primer 6 from FIG. 12B

Underline italics = 3' splice site sequence from FIG. 9B

Bold italics = primer 7 from FIG. 12B

RECORDED IN THE U.S. PATENT AND TRADEMARK OFFICE